J. Math. Biol. (1991) 29: 195–217

Journal of
Mathematical
Biology

Multiple pulse interactions and averaging in systems of coupled neural oscillators*

G. B. Ermentrout[1] **and N. Kopell**[2]

[1] Department of Mathematics, University of Pittsburgh, Pittsburgh, PA 15260, USA

[2] Department of Mathematics, Boston University, Boston, USA

Received November 28, 1989; received in revised form April 6, 1990

Abstract. Oscillators coupled strongly are capable of complicated behavior which may be pathological for biological control systems. Nevertheless, strong coupling may be needed to prevent asynchrony. We discuss how some neural networks may be designed to achieve only simple locking behavior when the coupling is strong. The design is based on the fact that the method of averaging produces equations that are capable only of locking or drift, not pathological complexity. Furthermore, it is shown that oscillators that interact by means of multiple pulses per cycle, dispersed around the cycle, behave like averaged equations, even if the number of pulses is small. We discuss the biological intuition behind this scheme, and show numerically that it works when the oscillators are taken to be composites, each unit of which is governed by a well-known model of a neural oscillator. Finally, we describe numerical methods for computing from equations for coupled limit cycle oscillators the averaged coupling functions of our theory.

Key words: Oscillations – Neurons – Averaging – Neural circuits

1. Introduction

Many physiological control systems are governed by coupled neural oscillators [1–4]. In these systems, it is important to maintain some degree of synchronization. In order to maintain synchrony, coupling between the oscillating units must be sufficiently strong; weak coupling can synchronize only oscillators that are very close in natural frequency. If the difference between units is too great and coupling is weak, desynchronous behavior can arise, such as phase drift [5]. On the other hand, if the coupling is too strong various pathological situations arise. For example, in [6] it is shown that strong diffusive coupling between chemical

* Research partially supported by the National Science Foundation under grants DMS 8796235 and DMS 8701405 and the Air Force Office of Scientific Research under University Research Contract F 49620-C-0131 to Northeastern University

oscillators can lead to chaos. Similarly, we have found that strong inhibitorily coupled neural oscillators can sometimes lead to complex dynamical behavior [unpublished]. In a previous paper [7], we showed that mutual excitatory coupling of sufficient strength between a pair of limit cycle oscillators can act to stop the oscillation ("oscillator death"). The mechanism described in [7] can occur in models of neural interactions that involve chemical synapses even if the neural oscillators are identical. We are thus faced with the following problem: How can we maintain synchrony between possibly disparate oscillators without strengthening the coupling so much as to cause loss of oscillation or other dynamic pathologies?

We show in [7] that oscillator death cannot occur if the oscillators are weakly coupled. When coupling is weak, invariant manifold theory may be used to reduce the system of nonlinear oscillators to a set of equations on a torus. Averaging theory may then be used to obtain equations that depend only on the *differences* of the phases of the oscillators. For a pair of oscillators the averaged equations have only two possible behaviors: synchronization or quasiperiodic oscillations (phase drift). The latter occurs if the uncoupled frequencies of the oscillators are not sufficiently close to one another.

In this paper we show that, even with strong interactions, the system may behave as if averaged, and we describe some neural networks that can accomplish this. The fundamental idea is that, if interactions are dispersed around the cycle of the oscillators, the system can behave as though the coupling were averaged over a cycle, and thus all of the above pathological behavior is prevented. For such a system, the coupling can be strong enough to overcome many frequency inhomogeneities that could otherwise lead to phase drift.

The paper is organized as follows: in Sect. 2, we review the derivation of phase models from the full system of oscillators. We then discuss how phase equations modelling a pair of coupled oscillators may be *formally* averaged, and when this averaging method is valid. In Sect. 3 we show that, if the coupling consists of a sum of terms each corresponding to a pulse, and if these pulses are sufficiently dispersed around the cycle, then the averaging method is valid for a sufficiently large number of pulses. We also discuss the biological intuition behind the multiple pulse coupling, and how such coupling is naturally obtained when the oscillator is a composite of neurons, possibly with different cell types. Numerical calculations are done in Sect. 4 to show that even a small number of pulses (e.g. 3 or 4) may be enough to radically change the behavior of the coupled system, from one that undergoes "oscillator death" if the interaction is only by a single pulse to one that phase-locks like a system whose coupling depends only on the differences on the phases.

The composite oscillators of the networks of Sect. 3 have elements that are very tightly coupled compared to the inter-oscillator coupling. In Sect. 5, we show numerically the requirement for tight intra-oscillator coupling can be relaxed and still have the system behave without pathology. This is done both for phase models (reduced from full equations describing amplitudes as well as phases) as well as the full equations, and allows the construction of "averaging networks" that are more physically realistic and more general.

In the appendix, we consider numerical methods for computing an approximation to the averaged coupling functions H (which depend only on the phase difference $\phi \equiv \theta_2 - \theta_1$). $H(\phi)$ is computed under two alternative hypotheses. In the first, the limit cycle has "infinite" attraction but the coupling need not be weak; in the second, the rate of attraction to the limit cycle is finite, but the coupling is weak. In the first case, one uses the numerical techniques to first reduce to a phase model and then to average. In this situation, when the attraction is extremely strong, the dependence of the local frequency on the amplitudes Y_i is not very important. In the second case, in which the attraction need not be extremely strong, the dependence of $d\theta_i/dt$ on the amplitudes may not be ignored. This is a more subtle calculation, which is done in two ways. We apply our method to a class of neural equations that include the Lecar–Morris system [8] and the Wilson–Cowan equations [9].

2. Reduction to phase models and averaging

2.1. Reduction to phase models

For completeness, we briefly review the reduction of a pair of coupled oscillators to a system of equations on the torus. Consider the coupled system of nonlinear oscillators:

$$\begin{aligned} dX_1/dt &= F_1(X_1) + \beta G_1(X_1, X_2), \\ dX_2/dt &= F_2(X_2) + \beta G_2(X_2, X_1). \end{aligned} \tag{2.1}$$

Here $X_j \in \boldsymbol{R}^n$, β is a parameter determining the strength of coupling between the two oscillators, G_j is the coupling function, and it is assumed that $dX_j/dt = F_j(X_j)$ has as a solution an orbitally asymptotically stable periodic solution with frequency ω_j. In [10] it is shown that there is a change of coordinates in the neighborhood of the limit cycle such that, if β is not too large, (2.1) can be written as

$$\begin{aligned} \omega_j^{-1}\, d\theta_j/dt &= 1 + q_j(y_j, \theta_j) + \beta c_j(y_j, y_k, \theta_j, \theta_k, \beta), \\ dy_j/dt &= a_j(y_j, \theta_j) + \beta d_j(y_j, y_k, \theta_j, \theta_k, \beta), \end{aligned} \tag{2.2}$$

$j, k = 1, 2, j \neq k$ (see also the appendix). Here $q_j(0, \theta) = a_j(0, \theta) = 0$, and all functions are periodic in their θ arguments. The coordinates $y_i \in \boldsymbol{R}^{n-1}$ are transverse to the periodic orbits and $\theta_j \in S^1$ lies along the limit cycle of the jth oscillator. In absence of coupling ($\beta = 0$) each oscillator traverses its cycle with a period of $2\pi/\omega_j$. There are two situations in which we can reduce (2.2) from a $2n$-dimensional system to a flow on a two-dimensional torus. If β and $|F_1 - F_2|$ are sufficiently small, we can use invariant manifold theory [11] to construct a torus $y_j(\theta_j, \theta_k)$ which is invariant for (2.2). On that torus, the equations have the form

$$\omega_j^{-1}\, d\theta_j/dt = 1 + \beta h_j(\theta_j, \theta_k, \beta), \tag{2.3}$$

$j, k = 1, 2, j \neq k$. If $|\omega_j - \omega_k| = O(\beta)$, then averaging theory [12] implies that there is an almost identity change of coordinates such that, in the new variables, (2.3) has the form

$$\omega_j^{-1}\, d\theta_j/dt = 1 + \beta H_j(\theta_k - \theta_j) + O(\beta^2). \tag{2.4}$$

Here, H_j is a 2π-periodic function of its arguments. If $\phi = \theta_2 - \theta_1$, the functions H_j are determined from h_j by

$$\begin{aligned} H_1(\phi) &= (1/2\pi) \int_0^{2\pi} \beta h_1(\theta_1, \theta_1 + \phi, \beta)\, d\theta_1, \\ H_2(-\phi) &= (1/2\pi) \int_0^{2\pi} \beta h_2(\theta_2, \theta_2 - \phi, \beta)\, d\theta_2. \end{aligned} \tag{2.5}$$

The second situation in which (2.2) can be reduced to a flow on the torus is if the attraction to the limit cycle is strong (see [7]). Strong attraction implies that $\{y_j\}$ remain close to 0, so that (2.2) reduces to

$$\omega_j^{-1}\, d\theta_j/dt = 1 + \beta h_j(\theta_j, \theta_k, \beta), \tag{2.6}$$

where now $h_j(\theta_j, \theta_k, \beta)$ is given explicitly by $\omega_j c_j(0, 0, \theta_j, \theta_k, \beta)$.

In the absence of the $O(\beta^2)$ terms, (2.4) is capable only of phase-locking or phase-drift. Equations of the form (2.6) are more general, and are capable of considerably more complex behavior, including a variety of locking patterns and oscillator death [7]. The latter is very easy to obtain, particularly when h_1, h_2 are derived from excitatory neural coupling (see [7]). If the coupling is sufficiently strong that the averaging theorem cannot be applied to produce (2.4), we are confronted by the problems discussed in the introduction.

Remark 2.1. In [7], we show that for some models of excitatory neural coupling, the functions $h_j(\theta_j, \theta_k, \beta)$ have the form $P_j(\theta_k)R_j(\theta_j)$ where $P(\theta)$ is a positive pulse-like function and $R(\theta)$ is analogous to the phase-response curve for a forced oscillator. (See [7] and [1].)

2.2. *Averaging*

If β is small, averaging theory provides an almost identity change of coordinates such that, in the new coordinates, the coupling depends only on the difference ϕ of the phases. Even if β is not small, one may rewrite (2.6) by *formally* averaging, leaving a remainder term:

$$\begin{aligned} d\theta_1/dt &= \omega_1 + H_1(\phi) + F_1(\theta_1, \theta_2), \\ d\theta_2/dt &= \omega_2 + H_2(-\phi) + F_2(\theta_2, \theta_1), \end{aligned} \tag{2.7}$$

where $\phi = \theta_2 - \theta_1$, H_1, H_2 are as in (2.5) and

$$F_1(\theta_1, \theta_2) = \beta h_1(\theta_1, \theta_2, \beta) - H_1(\theta_2 - \theta_1),$$

$$F_2(\theta_2, \theta_1) = \beta h_2(\theta_2, \theta_1, \beta) - H_2(\theta_1 - \theta_2).$$

Let $M = \max_{\theta_1, \theta_2} |F_j(\theta_j, \theta_k, \beta)|, j, k = 1, 2; j \neq k$. If M happens to be sufficiently small (as is automatically true if β is small), the consequences of averaging theory for small β still hold. For example:

Proposition 2.1. *Suppose that*

$$\frac{d\phi}{dt} = \omega_1 - \omega_2 + H_1(\phi) - H_2(-\phi) \tag{2.8}$$

has a hyperbolic fixed point, where $\phi = \theta_2 - \theta_1$. Then for M sufficiently small, (2.7) *has a hyperbolic limit cycle of the same stability characteristics.*

Proof. A critical point of (2.8) corresponds to a periodic solution of

$$\begin{aligned} d\theta_1/dt &= \omega_1 + H_1(\phi), \\ d\theta_2/dt &= \omega_2 + H_2(-\phi). \end{aligned} \tag{2.9}$$

Consider a Poincaré section through that periodic solution and take the same section for (2.7). Then for M sufficiently small, the Poincaré map of (2.7) is still defined and is close to that of (2.9). Therefore, it has a hyperbolic fixed point with the same stability characteristics. □

Since M represents the deviation from being averaged, we refer to it as the "modulus of averageability". A system with a low modulus cannot undergo "oscillator death", i.e. (2.9) has no critical points. That is, by continuity we have

Proposition 2.2. *Suppose that* $|(d\theta_1/dt, d\theta_2/dt)|$ *of* (2.9) *is bounded away from zero. (This is true for generic* ω_1, ω_2.) *Then for M sufficiently small,* (2.7) *has no critical points.* □

Remark 2.2. The above propositions also work for chains of N oscillators. The kth equation is averaged over θ_k, with $\theta_{k+1} = \phi_k + \theta_k$ and $\theta_{k-1} = \theta_k - \phi_{k-1}$. The averaged system is then a function of only the phase differences $\{\phi_k\}$. The main hypothesis, as in the above theorem, is that the maximum over the N-torus of the difference between the true R.H.S. of the equation and that of the averaged right-hand side (considered as a function of $\{\theta_k\}$) be sufficiently small.

3. Multiple pulses and the reduction of the modulus of averageability

In the last section, we noted that if the phase equations (2.7) are close enough to the averaged equations, then their behavior is also similar. Here we shall describe some networks of oscillators which exploit this fact. These networks are designed so as to distribute the impulses over the cycle of the oscillation, rather than concentrating them near one particular phase of the cycle. As we shall see, these networks behave like "averaged" equations, and hence avoid the problems described above.

Consider a pair of oscillatory units and assume that these units are composed, not of a single pacemaker, but rather of m oscillating subunits. (These subunits need not be capable of oscillating in isolation.) For example, it is believed that the segmental oscillators of the leech central pattern generator consists of at least four subunits that oscillate. (See [3] for a 1978 version of the local oscillator; since then, other oscillating components have been discovered (M. Nussbaum, pers. comm.).) We assume further that these subunits have fixed phase relationships to one another and do not all oscillate in phase; this can be accomplished using some inhibitory coupling (see Sect. 5). The coupling within a single unit is assumed to be sufficiently strong so that, if one of the units is phase-shifted by a stimulus, then the other subunits follow almost immediately.

Consider the following special example, in which each subunit of an oscillating unit synapses only on its analogue in the other oscillatory system. These assumptions are illustrated in Fig. 1. Let θ_1 denote the phase of a fixed oscillating subunit in one system and θ_2 denote the phase of the analogous subunit in the other system. Since we assume that all subunits in each system have fixed phase relations, θ_1 determines the phases of the remaining subunits: $\theta_1 + \xi_1, \ldots, \theta_1 + \xi_{m-1}$. We assume a similar relationship exists between θ_2 and

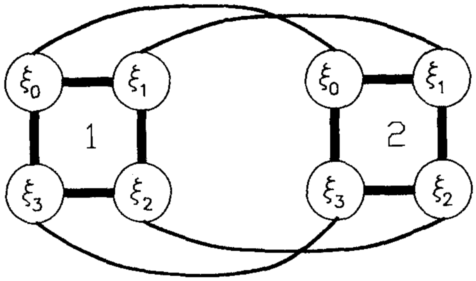

Fig. 1. A pair of oscillating networks, each consisting of four subunits. The phase relationships within a network are fixed, relative to $\xi_0 = 0$ in each oscillator

the other subunits in oscillator 2. The equations for this network are

$$\begin{aligned} d\theta_1/dt &= \omega_1 + \frac{1}{m}\sum_{i=0}^{m-1} h_1^i(\theta_1 + \xi_i, \theta_2 + \xi_1), \\ d\theta_2/dt &= \omega_2 + \frac{1}{m}\sum_{i=0}^{m-1} h_2^i(\theta_1 + \xi_i, \theta_1 + \xi_i). \end{aligned} \tag{3.1}$$

Here $\xi_0 = 0$. The sums in (3.1) arise out of our assumptions that resetting one subunit instantaneously resets the other units by an identical amount. The factor $1/m$ multiplying these sums is a normalization so that the total influence of one oscillating system on the other has magnitude independent of m. Note that if there is only a single unit or if all m units fire synchronously (i.e. $\xi_i = 0$) (3.1) is the same as (2.6). Thus, we may view equations of the form (3.1) as generalizations of our original phase model for two coupled oscillators. Suppose m is large, h_1^i is independent of i and the phases ξ_i have a density $\eta(\xi)$, i.e. the probability of ξ_i lying between ξ and $\xi + d\xi$ is $\eta(\xi)\, d\xi$. Then the sums in (3.1) converge to integrals as m tends to infinity:

$$S_m \equiv \frac{1}{m}\sum_{i=0}^{m-1} h_1(\theta_1 + \xi_i, \theta_2 + \xi_i) \to \int_0^{2\pi} h_1(x, x + \theta_2 - \theta_1)\eta(x - \theta_1)\, dx. \quad (3.2$$

In particular, if $\eta(\xi)$ is uniform, i.e., the phases are distributed equally around the circle, then $\eta(\xi) = 1/2\pi$ and (3.2) becomes

$$S_m \to \frac{1}{2\pi}\int_0^{2\pi} h_1(x, x + \theta_2 - \theta_1)\, dx, \tag{3.3}$$

which is just the averaged right-hand side as defined in (2.5), (2.9). This calculation shows:

Proposition 3.1. *If h_1^i and h_2^i are independent of i, and the pulses are uniformly distributed around the cycle, then the modulus M tends to* 0 *as the number of pulses m tends to* ∞. *Hence, the solutions to* (3.1) *are close to those of the averaged equations* (2.9) *as the number of subunits becomes large.* □

Remark 3.1. Even a small number of pulses ($m = 3$ or 4) causes a significant decrease in the modulus of averageability, and a dramatic change in the behavior of the system. This is detailed numerically in Sect. 4.

Remark 3.2. In order that M become small, it is not necessary that h_1^i and h_2^i be independent of i. It suffices that these functions be sufficiently similar for different values of i. Furthermore, it is easy to construct examples in which h_1^i, h_2^i are

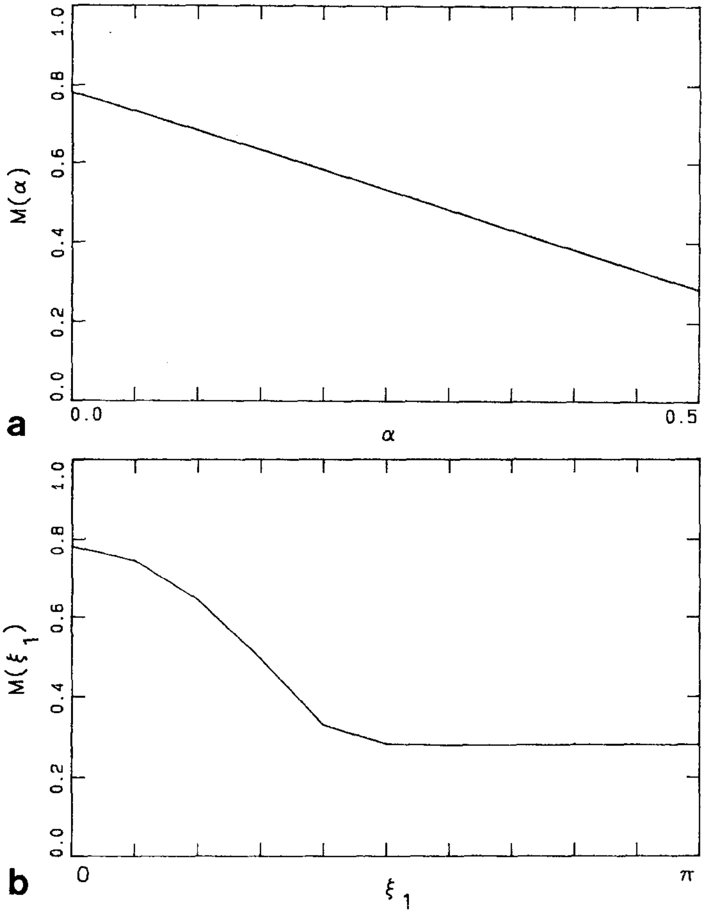

Fig. 2 a,b. Modulus of averageability for pulses of different strengths and phase shifts for the equation $\dot{\theta}_1 = \alpha P(\theta_2)R(\theta_1) + (1-\alpha)P(\theta_2+\xi_1)R(\theta_1+\xi_1)$; $P(\theta) = (\frac{1}{2}+\frac{1}{2}\cos\theta)^4$, $R(\theta) = \sin\theta$. **a** $\xi_1 = \pi$, α varies between 0 and $\frac{1}{2}$. Note that $\alpha = \frac{1}{2}$ is the case described in the proposition, $\alpha = 0$ corresponds to a single pulse; **b** $\alpha = \frac{1}{2}$, ξ_1 varies between 0 and π. $\xi_1 = 0$ corresponds to a single pulse and $\xi_1 = \pi$ in the case described in the proposition

quite different for different i, and the pulses are not uniformly distributed. For example, consider the simple case $h_1^1 = \alpha P(\theta_2)R(\theta_1)$, $h_1^2 = (1-\alpha)P(\theta_2+\xi_1)$ $R(\theta_1+\xi_1)$, with $P(\theta) = (\frac{1}{2}+\frac{1}{2}\cos\theta)^4$, $R(\theta) = \sin\theta$. As seen in Fig. 2, M is significantly decreased even if the two pulses are quite different in size ($\alpha \neq \frac{1}{2}$) or not uniformly distributed ($\xi_1 \neq \pi$).

Remark 3.3. Finally, it is not necessary that each subunit of an oscillator synapse only on its analogue. If subunit $I(i)$ of oscillator 1 responds to a pulse from subunit i of oscillator 2, then such a pulse contributes

$$P_i(\theta_2+\xi_i)R_i(\theta_1+\xi_{I(i)})$$

to the equation for $d\theta_1/dt$. The latter expression can be written as

$$P_i(\theta_2+\xi_i)\bar{R}_i(\theta_1+\xi_i),$$

i.e., a term of the form previously discussed, with a different response curve. It is now clear that the same principles allow one to construct "averaging networks" from composite oscillators, without requiring that the connections between the oscillators link only analogous subunits. One does require that the effective response functions $\bar{R}$ have the property that averaging them lowers variation from the mean over θ, as in the previous example.

4. Numerical results

In this section, we compare Poincaré maps for averaged systems of coupled oscillators to ones with multiple pulse, but unaveraged coupling. One of our main conclusions is that, even for highly nonlinear and discontinuous models using coupling by δ-functions, the number of pulses required for good agreement between the Poincaré maps is small (e.g., 3 or 4). We also compare the average phase difference over a cycle for some phase-locked unaveraged systems with the constant phase difference of the same systems when averaged. We find that there is little difference even if there is only one pulse per cycle, i.e., *in the range where these oscillators do not undergo death, they behave very much like their averaged counterparts.*

We shall work with phase equations coupled by pusles, where the phase equations are derived by assuming that the attraction to the limit cycle is very large, as seems to be the case for the Wilson–Cowan equations [9]. (See [7], §2, Remark 2.1.) If there are multiple pulses centered around phases $\xi_i, i = 1, \ldots, m$, the equations are

$$\begin{aligned} d\theta_1/dt &= \omega_1 + \frac{1}{m}\sum_{i=1}^{m} P(\theta_2 - \xi_i)R(\theta_1 - \xi_i), \\ d\theta_2/dt &= \omega_2 + \frac{1}{m}\sum_{i=1}^{m} P(\theta_1 - \xi_i)R(\theta_2 - \xi_i). \end{aligned} \tag{4.1}$$

We shall take $\xi_i = 2\pi i/m$, and

$$\begin{aligned} P(\theta) &= (0.5 + 0.5\cos(\theta))^n \quad \text{or} \quad \delta(\theta), \\ R(\theta) &= -\alpha[\sin(\theta + \eta) - \sin(\eta)]. \end{aligned} \tag{4.2}$$

Throughout these computations, we have set $n = 4$. Using repeated integration by parts, we find that the average function, as defined in Section 2, is

$$H(\phi) = I_n\alpha\left[\sin(-\phi + \eta) - \frac{n+1}{n}\sin(\eta)\right], \tag{4.3}$$

where

$$I_n = \frac{1}{2\pi}\int_{-\pi}^{\pi} P(\theta)\, d\theta = \frac{1\cdot 3\cdot 5\cdot \ldots \cdot 2n-1}{2\cdot 4\cdot 6\cdot \ldots \cdot 2n}.$$

In our first set of simulations, we fix all parameters ($n = 4$, $\eta = -\tan^{-1}(0.5)$, $\alpha = 2$) except for m, the number of pulses, and compare the Poincaré maps of (4.1) with those of the averaged equations (2.9), with $\omega_1 = 1$, $\omega_2 = 0.8$. $H_1 = H_2 = H$, with H given by (4.3). Figure 3a shows the Poincaré map taken at the $\theta_1 = 0$ section for $P(\theta) = \delta(\theta)$ and $m = 1$, along with that of the averaged equation; the two are quite dissimilar. However, for as few as 4 pulses per cycle

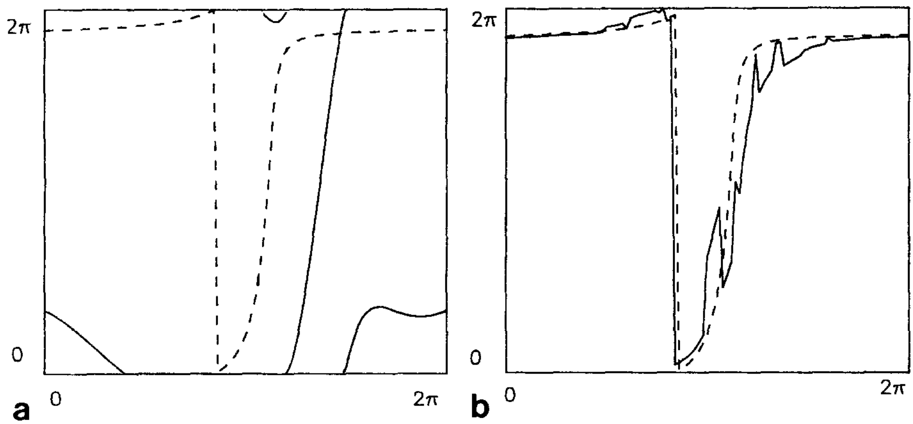

Fig. 3 a,b. Poincaré maps compared to the averaged analogues (*dashed*) for $\omega_1 = 1$, $\omega_2 = 0.8$, $P(\theta) = \delta(\theta)$, $R(\theta) = -2[\sin(\theta + \eta) - \sin(\eta)]$, $\eta = -\tan^{-1}(\frac{1}{2})$. **a** 1 Pulse per cycle; **b** 4 pulses per cycle

($m = 4$), there is a qualitative and quantitative similarity between the two, as can be seen in Fig. 3b. This result is typical. Figure 4 shows the Poincaré maps of (4.1) for $m = 1$ and $m = 4$, with $P(\theta)$ smooth as in (4.2) and $R(\theta)$ as defined in (4.2) ($\alpha = 1$, $\eta = -0.5$), along with that of the averaged equations for comparison. At $m = 1$, the map is quite different and phase shifted from that of the average, but for $m = 4$, the maps are very close. For higher values of m, the Poincaré map is indistinguishable from that of the averaged equations.

Suppose that we choose α large enough so that there is oscillator-death for (4.1) when $m = 1$ (i.e. $(\theta_1(t), \theta_2(t)) \to (\theta_1, \theta_2)$, a steady state). If we then add more pulses (increase m) it is possible to prevent oscillator death for the system of oscillators. A natural question is: How many pulses are required to prevent oscillator death for a given pair of oscillators? The answer to this question depends of course on the nature of the functions, $P(\theta)$, $R(\theta)$, the strength of coupling, α, and the frequencies ω_1 and ω_2. For purposes of illustration, we

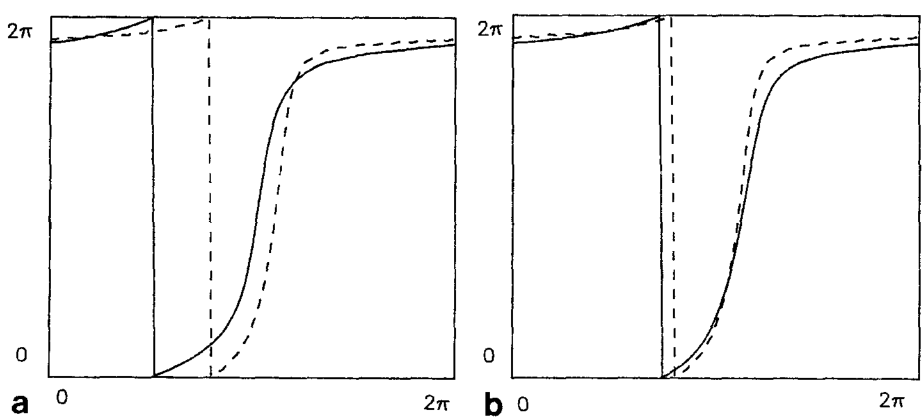

Fig. 4 a,b. Same as Fig. 3a,b, but $P(\theta) = (\frac{1}{2} + \frac{1}{2}\cos\theta)^4$. **a** 1 Pulse per cycle; **b** 4 pulses per cycle

Table 1. Maximum coupling strength and pulse number

m	α_m
1	2.43
2	4.88
3	8.20
4	17.92
5	38.08

consider the case of two identical oscillators and fix $\eta = -0.5$, $\omega_1, \omega_2 = 1.0$, $n = 4$, and let α vary. Table 1 shows the values of α at which at least m pulses are required to prevent oscillator death. Thus, if $\alpha < 2.43$, phase-death can never occur; for $2.43 < \alpha < 4.88$, at least two pulses are required to prevent death, etc. It is clear from the table that only a few pulses are required to prevent death, even with very strong coupling (strong relative to the size of the frequencies ω_1 and ω_2). We note that when α is large, and in the locking regime, the Poincaré maps for both the averaged equations and Eqs. (4.1) are quite flat in the sense that no matter what the initial condition is, after one cycle, the two oscillators have almost a zero phase-difference (thus, if $\Delta(\theta)$ is the Poincaré map, $\Delta(\theta) \approx 0$ for all θ).

In the next set of numerical calculations, we compare the average phase-difference between $\theta_2(t)$ and $\theta_1(t)$ with the phase-differences of the averaged equations when a stable phase-locked solution to (4.1) exists. We fix $\omega_2 = 1$ and let $\omega_1 \in (0, 1]$. We use $P(\theta)$, $R(\theta)$ as in (4.2) ($P(\theta)$ smooth, $n = 4$, $\eta = 0.5$) and consider several different values for α. We will find the following behavior: for weak coupling, as the frequency ω_2 decreases there is a transition from locking to phase-drift; for strong coupling, the transition is from locking to oscillator-death.

For *any* averaged system, the phase-difference is constant when locking occurs, and if the model is of the form (4.2) it is easily found that the phase-difference $\phi = \theta_2 - \theta_1$ between the two averaged oscillators satisfies

$$\sin(\phi) = \kappa(\omega_2 - \omega_1),$$

where κ is a constant depending on all of the parameters. Thus, if $\sin(\phi)$ is plotted as a function of ω_1 and ω_2 fixed at 1, a straight line is obtained. We define the average phase-difference between two phase-locked oscillators by

$$\langle\phi\rangle \equiv \frac{1}{T}\int_0^T \theta_2(t) - \theta_1(t)\, dt,$$

where T is the period of the phase-locked system. If θ_2 and θ_1 satisfy averaged equations of the form (2.7), then $\langle\phi\rangle = \phi = \theta_2(t) - \theta_1(t)$, a constant. In the following figures, we plot $\sin(\langle\phi\rangle)$ versus ω_1 for $m = 1$ and 3 values of the coupling strength α. In Fig. 5a, $\alpha = 1$; α is sufficiently small so that both the averaged and the unaveraged equations lose locking at a value of ω_1 in the interval [0.5, 1]. We have marked the critical value of the frequency at which locking is lost for the averaged and unaveraged systems. Because α is "small", it is not surprising that the average phase-differences between the two oscillators are similar for the averaged and unaveraged systems.

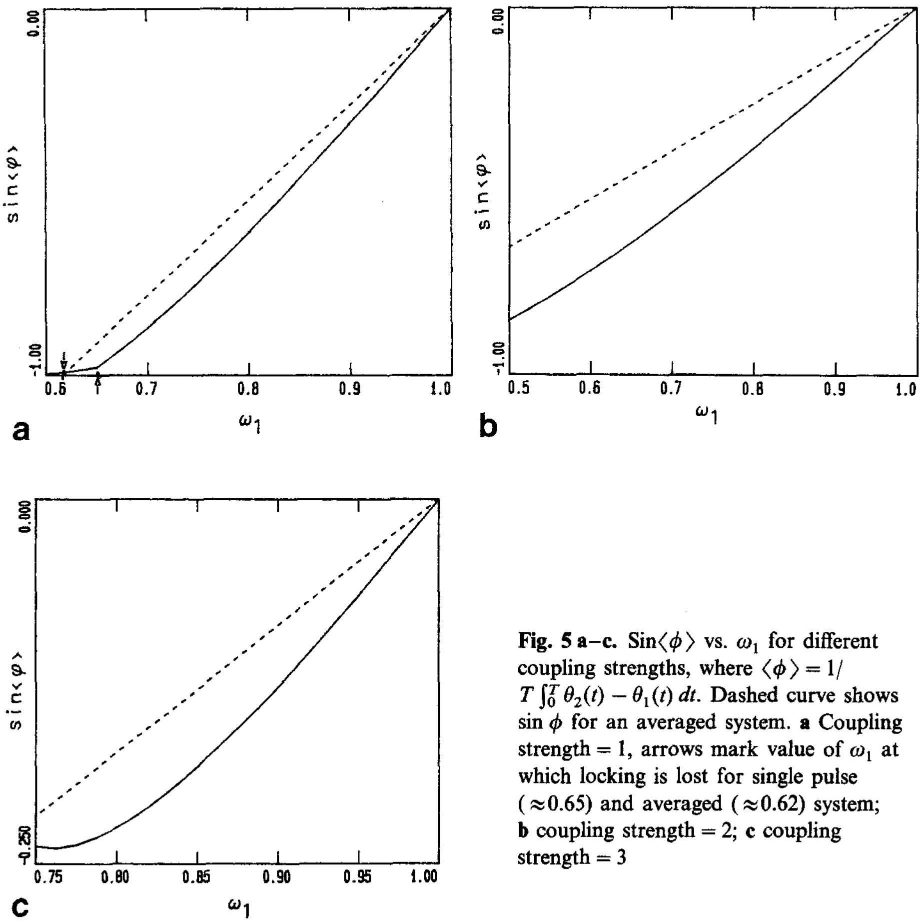

Fig. 5 a–c. Sin$\langle\phi\rangle$ vs. ω_1 for different coupling strengths, where $\langle\phi\rangle = 1/T\int_0^T \theta_2(t) - \theta_1(t)\,dt$. Dashed curve shows $\sin\phi$ for an averaged system. **a** Coupling strength = 1, arrows mark value of ω_1 at which locking is lost for single pulse (≈ 0.65) and averaged (≈ 0.62) system; **b** coupling strength = 2; **c** coupling strength = 3

Figure 5b has parameters identical to Fig. 5a except that the coupling is twice as strong ($\alpha = 2$). The coupling is still sufficiently weak so that oscillator-death does not occur for $0.5 \leqslant \omega_1 \leqslant 1$. Finally, in Fig. 5c we shall show the average phase-difference when $\alpha = 3$. At the critical value, $\omega_1 \approx 0.75$, oscillator death occurs for (4.1) so that there are no periodic solutions for smaller values of ω_1.

In the last simulation, we fix $\alpha = 6$ so that there is oscillator-death for any value of $\omega_1 \leqslant 1$ when $m = 1$. The coupling is now by 4 pulses ($m = 4$), which prevents the oscillator death, and we show three curves in Fig. 6 as ω_1 varies from 1.0 down to 0.1. These curves are $\sin(\langle\phi\rangle)$, $\sin(\phi_{\max})$, and $\sin(\phi_{\min})$, where $\phi_{\max}$ (resp. $\phi_{\min}$) $= \max_{0<t\leqslant T} \theta_2(t) - \theta_1(t)$ (resp. $\min_{0<t\leqslant T} \theta_2(t) - \theta_1(t)$). We have omitted the curve $\sin(\phi)$, since within the resolution of the graphical output, the curves $\sin(\phi)$ and $\sin(\langle\phi\rangle)$ are coincident. This figure shows that with as few as 4 pulses per cycle, Eq. (4.1) behaves almost exactly like its averaged analogue; indeed, the maximum and the minimum phase-differences are almost the same as the average phase-difference, so that $\theta_2(t) - \theta_1(t)$ is close to a constant.

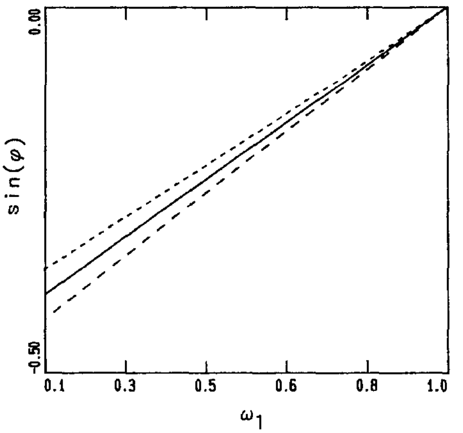

Fig. 6. Same as Fig. 5a–c but coupling - strength = 6, 4 pulses per cycle showing $\sin \phi_{\max}$, $\sin \phi_{\min}$, $\sin\langle\phi\rangle$, where $\phi_{\max} = \max_{0 \leqslant t \leqslant T} \theta_2(t) - \theta_1(t)$, $\phi_{\min} = \min_{0 \leqslant t \leqslant T} \theta_2(t) - \theta_1(t)$, $\langle\phi\rangle = 1/T \int_0^T \theta_2(t) - \theta_1(t)\,dt$. Small dashes are used for $\phi_{\max}$, large for $\phi_{\min}$, solid for $\langle\phi\rangle$

5. Realistic networks and stable distribution of phases

In Sect. 3, we showed that if a network is able to stably distribute phases about its cycle, then it is possible to obtain 1 : 1 locking and nearly averaged behavior with strong interactions between oscillators. This averageability is shown to prevent oscillator-death and other complex dynamical behavior. Two assumptions are implicit in the creation of these networks. First, we have assumed that we can arrange coupling within the network so that the cells within the network fire out of phase. Second, we have assumed that the interaction with another similar network does not disrupt this firing pattern. That such networks are realizable is not obvious. In this section, we show two examples, a phase model and a neural model, that exhibit the desired properties: (i) within the network, the oscillators are phase-shifted so that there is uniform dispersion of phases, and (ii) when two such networks are coupled, it is possible to obtain stable 1 : 1 locking even though the two oscillations are far apart in frequency.

5.1. Phase models

The most obvious way to set up a pattern of phases is to arrange the units of the network in a geometric ring and attempt to form a travelling wave that cycles the ring. If the "wavelength" is m, where m is the number of units in the ring, then the phases must necessarily be a multiple of $2\pi/m$ apart. A wavelength of 0 corresponds to synchronous oscillations in the ring. Other wavelengths correspond to nearest neighbor phase-lags of $2\pi/k$ where k is a divisor of m. In [13], it is shown that oscillators that are coupled in a ring with some "inhibition" have as stable solutions waves of the desired form. Furthermore, if the "inhibition" is strong enough, the synchronous solution of the ring is unstable—the phases necessarily separate. (A more explicit definition of such inhibition is given below.) The model analyzed in [13] has the form

$$\theta_j' = \omega + \sum_{i=0}^{m-1} H(\theta_i - \theta_j, i - j), \qquad j = 0, \ldots, m. \tag{5.1}$$

Since we are showing that, even if the interactions are not via phase-differences, the networks can "average" to create similar behavior, we do not want to start with equations of the form (5.1). Instead we will keep the ring geometry and consider a generalization of (5.1):

$$\theta_j' = \omega + \sum_{i=0}^{m-1} h(\theta_i, \theta_j, i-j), \qquad j = 0, \ldots, m. \tag{5.2}$$

We have in mind the class of models derived in Sect. 2 under the assumptions of "infinite attraction" to the limit cycle. For this type of model,

$$h(\theta_i, \theta_j, i-j) = P(\theta_i)R(\theta_j)w(i-j), \tag{5.3}$$

where $P(\theta_i)$ is the "impulse" of the oscillator i causing the response $R(\theta_j)$ on oscillator j with weight $w(i-j)$. About $R(\theta_j)$, we assume that $R' < 0$ for a neighborhood of $\theta = 0$. Such an R is produced as discussed in Sect. 2 from neural models describing coupling via excitatory interactions, i.e., ones in which the voltage is increased in the target neuron. Inhibitory coupling leads to response functions R with $R' > 0$ near $\theta = 0$. Thus, we can model excitatory (resp. inhibitory) coupling using a fixed response function R satisfying $R'(0) < 0$ and letting the weights w be positive (resp. negative).

Equation (5.3) is derived from a ring of identical neurons that have strongly attracting limit cycles as solutions. Preliminary work indicates for the network (5.3) that if the coupling is "excitatory", then the in-phase solution $\theta_j(t) = \theta_i(t)\ \forall i, j$ is a stable solution to (5.3). We must avoid this, for otherwise the oscillators in the ring all synchronize and the network is equivalent to a single oscillator. Thus, we assume that some of the coupling in the ring is inhibitory.

We consider (5.2) and (5.3) coupled to another such ring with "excitatory" coupling between rings:

$$\begin{aligned} d\theta_1^j/dt &= \omega_1 + R(\theta_1^j)\left[\sum_{i=0}^{m-1} w(i-j)P(\theta_1^i) + \alpha P(\theta_2^j)\right], \\ d\theta_2^j/dt &= \omega_2 + R(\theta_2^j)\left[\sum_{i=0}^{m-1} w(i-j)P(\theta_2^i) + \alpha P(\theta_1^j)\right], \end{aligned} \tag{5.4}$$

where

$$P(u) = (0.5 + 0.5\cos(u))^4, \qquad R(u) = -(\sin(u + 0.4) - \sin(0.4)). \tag{5.5}$$

Each oscillator ring 1 is coupled to neighbors in the ring and to its analogue oscillator in ring 2. In absence of coupling between rings ($\alpha = 0$), we choose $w(k)$ so that there is a wave in each ring. In the numerical experiment with ring structure, we have chosen $m = 6$, $w(0) = 0$, $w(1) = w(-1) = 0.1$, $w(2) = w(-2) = -0.6$, and $w(3) = -0.2$, $\omega_1 = 1$, and $\omega_2 = 0.5$.

In the first numerical experiment we simply couple two oscillators without the ring structure (i.e., we let $w \equiv 0$). For α small there is no locking, as is expected since the frequencies are quite different. As α increases there is a complicated sequence of $n : m$ locking patterns for which $m < n$. That is, there are always more cycles of the fast oscillator 1 than there are of the slow oscillator 2. At a particular value of α ($\alpha \approx 1.65$), oscillator 2 "stops"; that is, it no longer traverses a complete cycle. Oscillator 1 continues to traverse the cycle and this behavior persists for all higher values of α. Thus oscillator 1 and 2 do not ever lock in a 1 : 1 manner.

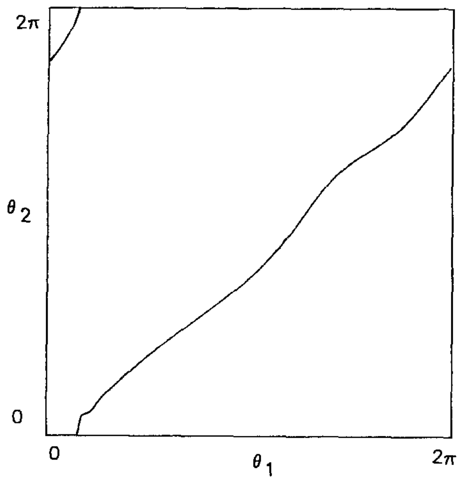

Fig. 7. θ_1^0 vs. θ_2^0 for $\alpha = 2$. Note that trajectory is close to straight line, i.e. $\theta_2^0 - \theta_1^0$ is almost independent of t

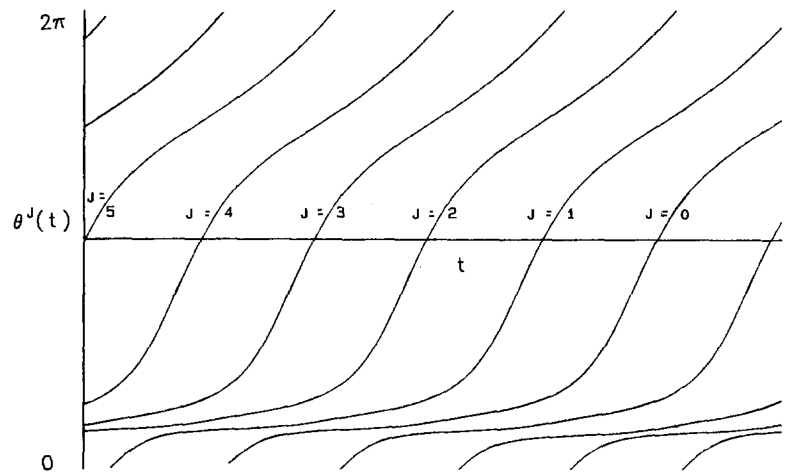

Fig. 8. $\theta_j^0(t)$ vs. t. Note that the wave structure is maintained even if the coupling between rings is moderately strong

In the second experiment we use the ring structure. For α small, there is again no locking. As we increase α we find that 1 : 1 locking occurs. In Fig. 7, we show the phase-plane diagram of θ_1^0 vs θ_2^0 for $\alpha = 2$. Note that the trajectory is nearly a straight line, indicating that the system is behaving as if it were averaged. In Fig. 8, we show the time-dependence of the trajectories for each of the phases. This figure shows that even with "strong" coupling between the rings, the phase relationships within a ring are preserved. We further note that the intra-ring coupling is small compared to the coupling between rings; thus we do not need to assume that the coupling within the ring is much stronger.

Finally, one might argue that it is the presence of inhibitory coupling within the ring rather than the existence of phase-shifts that is responsible for preventing the "oscillator death" of the coupled system. To see if this is the case, we consider the following variation of (5.4):

$$
\begin{aligned}
d\theta_1/dt &= \omega_1 + R(\theta_1)\left[\sum_{i=0}^{m-1} w(i)P(\theta_1) + \alpha P(\theta_2)\right],\\
d\theta_2/dt &= \omega_2 + R(\theta_2)\left[\sum_{i=0}^{m-1} w(i)P(\theta_2) + \alpha P(\theta_1)\right].
\end{aligned}
\tag{5.6}
$$

Equation (5.6) is just the symmetric form of (5.4), that is, $\theta_1^j = \theta_1$ for all j and similarly for θ_2^j. (Note that the symmetric solution is unstable as a solution to (5.4).) As in the first case, numerical experiments indicate that 1 : 1 locking is still impossible and a sequence of bifurcation similar to that without the ring structure occurs. For α large enough, oscillator 2 is stopped.

We have done similar numerical experiments for different parameters and different numbers of oscillators in the ring and find the same behavior within some limits. Obviously, if α becomes too large (well beyond the values that yield 1 : 1 locking in the rings), then oscillator death can and does occur.

5.2. Neural net models

In this section, we study two coupled rings of Wilson–Cowan neural equations:

$$
\begin{aligned}
dE_1^j/dt &= -E_1^j + f_e(\beta_{ee}^1 E_1^j - \beta_{ie} I_1^j + \alpha E_2^j),\\
dI_1^j/dt &= -I_1^j + f_i\left(\beta_{ei}E_1^j - \beta_{ii}I_1^j - \sum_{k=0}^{m-1} w(k-j)I_1^k\right),\\
dE_2^j/dt &= -E_2^j + f_e(\beta_{ee}^2 E_2^j - \beta_{ie} I_2^j + \alpha E_1^j),\\
dI_2^j/dt &= -I_2^j + f_i\left(\beta_{ei}E_2^j - \beta_{ii}I_2^j - \sum_{k=0}^{m-1} w(k-j)I_2^k\right), \qquad j = 0, \ldots, 5
\end{aligned}
\tag{5.7}
$$

Here E_j and I_j refer to populations of excitatory and inhibitory neurons. For $m = 1$ and coupling coefficients $\alpha = 0$ the system of E_1, I_1 (resp. E_2, I_2) forms an oscillator. The justification for the form of (5.7) can be found in other articles [9]. Coupling *within* the ring is soley through the *inhibitory* neurons I_j. Coupling *across* the two rings is through the *excitatory* neurons. Both rings are identical with the exception of the parameter, β_{ee}, which is different in the two rings. This parameter has a large effect on the intrinsic frequency of the oscillators, so it is varied in order that the uncoupled systems have different frequencies. The parameters used in our experiments are as in the caption to Fig. 9. There are three experiments as in the phase model.

In the first experiment, we allow (5.7) to evolve from random initial conditions. We find a large range of coupling strengths α that lead to 1 : 1 entrainment with no distortion in the wave shapes. Figure 9 shows the excitatory variables $E_1^0(t)$ and $E_2^0(t)$. Note that the faster oscillator is slightly advanced. The other component oscillators have identical profiles but they are phase-shifted. In Fig. 9b, we show the complete set of waves from network 1. Note that the phase relationships are not distorted by the coupling between the rings.

In the next experiment, we try to entrain the two oscillators without exploiting the ring structure. For this experiment, $w(k) \equiv 0$. We find that for α small, there is no locking; rather the two oscillations undergo quasi-periodic

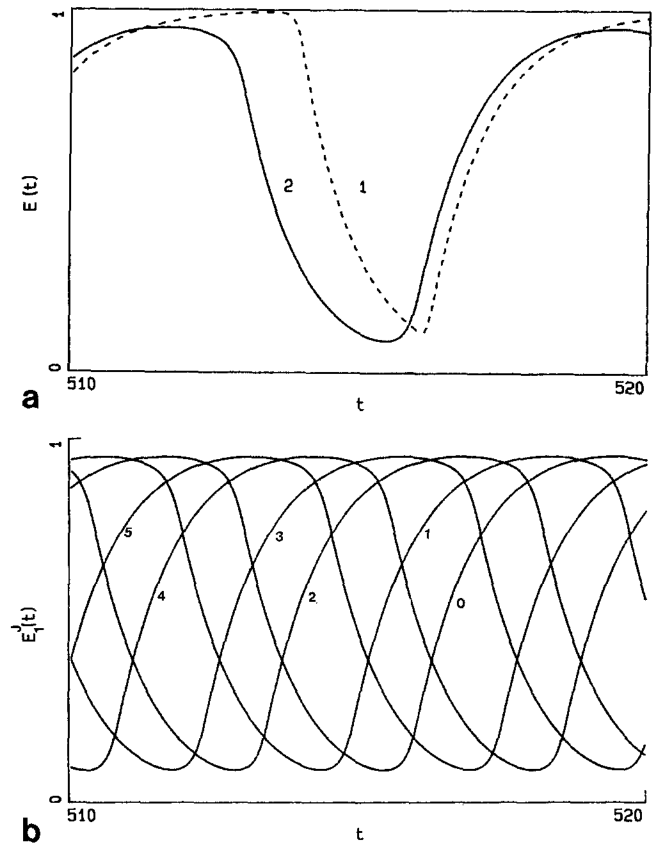

Fig. 9. a. Wilson–Cowan networks coupled together. $E_1^0(t)$ and $E_2^0(t)$ are plotted for one locked cycle. $\beta_{ee}^A = 12$, $\beta_{ee}^B = 18$, $\beta_{ii} = 0$, $\beta_{ie} = 20$, $\beta_{ei} = 18$, $w(0) = 0$, $w(1) = w(-1) = 0.1$, $w(2) = w(-2) = 2$, $w(3) = 0.3$; $f_e(u) = \frac{1}{2}(1 + \tanh(u - \frac{1}{2}))$; $f_i(u) = \frac{1}{2}(1 + \tanh(u - 4))$; $\alpha = 10$. **b** $E_1^j(t)$. Note that the waves persist after coupling

behavior. As α increases, there are regimes of periodic $n : m$ locking for $n \neq m$, separated by quasi-periodic and "chaotic" behavior. At $\alpha \approx 10$, the solutions appear to be "chaotic" and as α increases they become periodic and "burst-like" (several spikes repeated). At $\alpha \approx 10.5$ there is $1:1$ locking but this persists only until $\alpha \approx 10.58$ at which point all oscillations are stopped. The regime for $1:1$ locking is very small and depends a great deal on the parameters β_{ee}^1 and β_{ee}^2.

Finally, we perform the experiment analogous to the third experiment above in order to convince ourselves that it is in fact the intra-ring phase shifts, not the presence of inhibitory coupling, that are responsible for our ability to obtain $1:1$ locking. Thus, we consider the modified version of (5.7) where $(E_1^j, I_1^j) = (E_1^i, I_1^i)$ and $(E_2^j, I_2^j) = (E_2^i, I_2^i)$. Here, we *do* find a slim range of coupling strengths for which $1:1$ locking is possible but the wave forms are severely distorted; the faster oscillator has a small residual spike that appears to be a residue of a $2:1$ locked state.

These numerical results are only preliminary and by no means exhaustive; our goal here is to show that networks that can produce averaged interactions are simply constructed. These interactions appear to make it much easier for the two oscillators to entrain over a large range of coupling strengths and intrinsic frequencies without significantly distorting the waveforms of the oscillations. In a later paper, we will systematically explore models that are variations of (5.4) and (5.7).

Acknowledgement. We wish to thank L. Glass, whose resolute disbelief provoked us to back up some of our claims.

Appendix: Computation of the averaged functions

We describe in more detail the change of coordinates discussed in Sect. 2 in order to obtain explicit information about the functions in (2.2). We then use this information to derive numerical techniques for obtaining the averaged equations (2.4) when there is weak coupling and the functions $h_k(\theta_k, \theta_j)$ of (2.6) when the attraction to the limit cycle is very strong. We will see that the case of weak coupling is considerably more difficult, essentially because the properties of the equations off the limit cycles can affect the averaged equations, and we do that derivation in two ways. (See [10] and the appendix of [14] for related calculations.) Finally, we apply the methods to a class of neural models.

A1. Oscillators with strongly attracting limit cycles

Consider the pair of coupled oscillators (2.1). We assume as before the $dX_k/dt = F_k(X_k)$ has an asymptotically stable limit cycle solution which we shall call $U_k(t/\omega_k)$, where ω_k is the frequency of the limit cycle and $U_k(\theta)$ is 2π-periodic in its argument. Let $u_k = T_k(\theta_k, y_k)$, $y_k \in R^{n-1}$, be the coordinate transformations. These transformations can be chosen so that

$$u_k(t) = U_k(\theta_k(t)) + M_k(\theta_k(t))y_k(t) + O(|y_k^2|), \tag{A1}$$

where $M_k(\theta)$ is an $n \times (n-1)$ matrix and

$$\begin{aligned} M_k(\theta)^T M_k(\theta) &= 1_{(n-1)\times(n-1)}, \\ U_k'(\theta)^T M_k(\theta) &= 0_{1\times(n-1)}. \end{aligned} \tag{A2}$$

In the appendix to [7] it was shown that θ_k, y_k satisfy

$$\begin{aligned} \omega_k^{-1}\, d\theta_k/dt &= 1 + \varrho_k^{-1}(U_k')^T[(D_k + (D_k)^T)M_k y_k + G_k], \\ \omega_k^{-1}\, dy_k/dt &= ((M_k)^T D_k M_k + (M_k')^T M_k)y_k + (M_k)^T G_k. \end{aligned} \tag{A3}$$

(Here ω_k^{-1} arises from differentiation of $U_k(\theta_k/\omega_k)$ with respect to time.) We will use (A3) as the basis for the rest of the calculations in this appendix.

In the limit of "infinite attraction" to the limit cycle, $y_k \to 0$, and (A3) becomes (2.6) with

$$h_k(\theta_k, \theta_j) = \omega_k \varrho_k^{-1}(\theta_k)(U_k')^T(\theta_k)G_k(U_k(\theta_k), U_j(\theta_j)). \tag{A4}$$

The significance of (A4) is that it allows us to compute an approximate phase model, which is more accurate the greater the strength of the attraction of the limit cycle. Furthermore, the averages in (2.7), (2.9) can be quickly and easily computed without first performing the reduction to a phase model:

$$H_k(\bar{\phi}) = \frac{1}{2\pi}\int_0^{2\pi} \omega_k \varrho_k^{-1}(t)(U_k')^T(t) G_k(U_k(t), U_j(t+\bar{\phi}))\, dt, \tag{A5}$$

where $\bar{\phi} = \theta_j - \theta_k$. (See [7] for computation of the relevant phase model.)

A2. Weak coupling

If the coupling is weak, Eqs. (2.1) may be directly averaged, instead of first reduced to a phase model and then averaged. It follows from invariant manifold theory that when the coupling is weak, there always exists an invariant torus [11]. However, unlike the first case, the invariant torus is not necessarily the product of the limit cycles, and so amplitude variations may affect the local frequencies. The "amplitude effects" make the calculation of the averaged functions $H(\phi)$ much more difficult, since we must deal with the complete n-dimensional system instead of restricting our averaging to the "phase" component. Our goal in the remainder of this section is to derive a general formula that will enable us to calculate the phase effects in weakly coupled oscillators.

In order to study weak coupling, we must assume that $F_k = F + O(\varepsilon)$ where $\varepsilon \ll 1$ and the $O(\varepsilon)$ terms contribute small frequency differences between the two oscillators. We replace G_k and εG_k and absorb the frequency differnce terms into the εG_k terms. We can assume with no loss in generality that, to lowest order, $\omega_k = 1$.

Method 1. We replace y_k by εs_k, since y_k will be $O(\varepsilon)$ on the invariant torus. Equation (A3) becomes

$$\begin{aligned} d\theta_k/dt &= 1 + \varepsilon[b(\theta_k)s_k + \varrho^{-1}(\theta_k)(U')^T(\theta_k)G_k(U(\theta_k), U(\theta_j))] + O(\varepsilon^2), \\ ds_k/dt &= a(\theta_k)s_k + M^T(\theta_k)G_k(U(\theta_k), U(\theta_j)) + O(\varepsilon). \end{aligned} \tag{A6}$$

where

$$\begin{aligned} b(\theta) &= \varrho^{-1}(U')^T(D + D^T)M, \\ a(\theta) &= M^TDM + (M')^TM. \end{aligned} \tag{A7}$$

Note that $a(\theta)$ and $b(\theta)$ depend only on the original limit cycle and do not depend on the form of the coupling. The solution to (A6) is $\theta_k = t + \hat{\theta}_k$ where $\hat{\theta}_k$ is constant to lowest order. From (A6), we obtain equations for $\hat{\theta}_k$ and s_k:

$$d\hat{\theta}_k/dt = \varepsilon[b(t)s_k(t; \bar{\phi}) + \varrho^{-1}(t)(U')^T(t)G_k(U(t), U(t+\bar{\phi}))] + O(\varepsilon^2), \tag{A8a}$$

$$ds_k/dt = a(t)s_k(t; \bar{\phi}) + M^T(t)G_k(U(t), U(t+\bar{\phi})) + O(\varepsilon), \tag{A8b}$$

where $\bar{\phi} = \hat{\theta}_j - \hat{\theta}_k$. On the invariant manifold $s_k = s_k(\theta_k, \theta_j) = s_k(t, t+\bar{\phi}) + O(\varepsilon)$, when, to lowest order in ε, $\bar{\phi}$ is constant. We write $s_k(t; \bar{\phi})$ to make this dependence explicit. We solve (A8b) for $s_k(t; \bar{\phi})$ and substitute this into (A8a). We are then in a position to average equation (A8a), yielding

$$d\hat{\theta}_k/dt = \varepsilon\tilde{H}_k(\theta_j - \theta_k),$$

where

$$\tilde{H}_k(\phi) = \frac{1}{2\pi}\int_0^{2\pi} b(t)s_k(t;\phi) + \varrho^{-1}(t)(U')^T(t)G_k(U(t), U(t+\phi))\,dt.$$

The function $\tilde{H}_k(\phi)$ consists of two components, one corresponding to the effects of amplitude on the local frequencies. The second component is identical to (A5), so the difference between the coupling function H_k for strong limit cycles and the true coupling function $\tilde{H}^k$ is the integral

$$\mathscr{H}_k(\phi) = \frac{1}{2\pi}\int_0^{2\pi} b(t)s_k(t;\phi)\,dt. \tag{A9}$$

H_k has the benefit that it does not depend on the coordinate matrix M_k, so that it is easily computed for arbitrary limit cycles. We now turn our attention to the computation of $\mathscr{H}_k$.

From a numerical standpoint, it is very wasteful to solve for s_k and substitute into (A9), since the value of s_k changes each time the coupling functions are changed. Furthermore, it is impractical to maintain the array s_k in memory since, for each of the $n-1$ components of s_k, one must store K^2 numbers if s_k is to be evaluated at K times and K values of ϕ. Instead, what is desired is a single vector function $U^*(t)$ that is independent of the coupling and is such that

$$\tilde{H}_k(\phi) = \frac{1}{2\pi}\int_0^{2\pi} U^{*T}(t)G_k(U(t), U(t+\phi))\,dt. \tag{A10}$$

Besides requiring less computer storage, the other advantage of U^* is that it need only be calculated once; $\tilde{H}_k$ can then be computed for arbitrary types of coupling. We will now show how such a function $U^*(t)$ can be computed. Let $E(t)$ satisfy

$$dE/dt = a(t)E, \qquad E(0) = I_{(n-1)\times(n-1)}, \tag{A11}$$

i.e., $E(t)$ is the exponential of $a(t)$. Let

$$Q(t) = \int_0^t b(\xi)E(\xi)\,d\xi. \tag{A12}$$

We rewrite (A9) as

$$\begin{aligned}\mathscr{H}_k(\phi) &= \frac{1}{2\pi}\int_0^{2\pi} b(t)E(t)E^{-1}(t)s_k(t;\phi)\,dt\\ &= \frac{1}{2\pi}\int_0^{2\pi} d/dt(Q(t))E^{-1}(t)s_k(t;\phi)\,dt\\ &= \frac{1}{2\pi}Q(2\pi)E^{-1}(2\pi)s_k(2\pi;\phi) - \frac{1}{2\pi}\int_0^{2\pi} Q(t)\frac{d}{dt}(E^{-1}(t)s_k(t;\phi))\,dt.\end{aligned} \tag{A13}$$

Note that $Q(t)$ does not depend on the coupling and is a function only of the normal coordinates and the limit cycle. To evaluate the last integral of (A13), we use the definition of $E(t)$ and (A8b) to obtain

$$\frac{d}{dt}[E^{-1}(t)s_k(t;\phi)] = E^{-1}(t)M^T(t)G_k(U(t), U(t+\phi)). \tag{A14}$$

Before substituting this into (A13), we need to find $s_k(2\pi;\phi)$. We integrate (A14) and use the fact that $s_k(2\pi; \bar{\phi}) = s_k(0; \bar{\phi})$. Thus,

$$s_k(2\pi; \bar{\phi}) = [I - E(2\pi)]^{-1} E(2\pi) \int_0^{2\pi} E^{-1}(t) M^T(t) G_k(U(t), U(t + \bar{\phi}))\, dt. \tag{A15}$$

Finally, we substitute (A14) and (A15) into (A13) to obtain

$$\begin{aligned}\mathscr{H}_k(\bar{\phi}) &= \frac{1}{2\pi} \int_0^{2\pi} \{Q(2\pi)[I - E(2\pi)]^{-1} - Q(t)\} E^{-1}(t) M^T(t) G_k(U(t), U(t + \bar{\phi}))\, dt \\ &\equiv \frac{1}{2\pi} \int_0^{2\pi} \eta^T(t) G_k(U(t), U(t + \bar{\phi}))\, dt. \end{aligned} \tag{A16}$$

(Note that we have used the fact that $E(t)$, $E^{-1}(t)$ and $[I - E(t)]^{-1}$ all commute in order to simplify (A16).) The vector function $\eta(t)$ is independent of the coupling as required. Our function $U^*(t)$ is

$$U^*(t) = [\varrho^{-1}(t) U'(t) \eta(t)]. \tag{A17}$$

Method 2. The above derivation of the functions $\tilde{H}_k(\bar{\phi})$ has a rather geometric flavor. Another approach is to use the Fredholm alternative and formal perturbation expansions. We will sketch this method below and show that the results are equivalent. Consider the coupled equations:

$$dX_k/dt = F(X_k) + \varepsilon G_k(X_k, X_j). \tag{A18}$$

One seeks solutions of the form $X_k(t) = U(t + \theta_k(\tau)) + \varepsilon W_k(t, \tau, \varepsilon)$, where $\tau = \varepsilon t$ is a slow time scale and $W_k(t, \tau, \varepsilon)$ is a smooth function of its components. Substitution of this formula into (A18) yields at order ε

$$\begin{aligned}\mathscr{L}(t + \theta_k) &\equiv [d/dt - D(t + \theta_k)] W_k(t, \tau, 0) \\ &= -U'(t + \theta_k)\, \partial\theta_k/\partial\tau + G_k(U(t + \theta_k), U(t + \theta_j)). \end{aligned} \tag{A19}$$

Periodic solutions W_k are sought. The linear equation

$$\mathscr{L}(t)\zeta(t) = f(t)$$

has a periodic solution if and only if

$$\int_0^{2\pi} \chi^*(t) f(t)\, dt = 0,$$

where $\chi^*(t)$ is the unique periodic solution to the adjoint problem

$$\begin{gathered}[d/dt - D^T(t)]\chi^*(t) \equiv \mathscr{L}^*(t)\chi^*(t) = 0, \\ \frac{1}{2\pi} \int_0^{2\pi} \chi^*(t) u'(t)\, dt = 1. \end{gathered} \tag{A20}$$

Thus, (A19) has a solution if and only if

$$\partial\theta_k/\partial\tau = \check{H}_k(\theta_j - \theta_k) \equiv \frac{1}{2\pi} \int_0^{2\pi} \chi^*(t) G_k(U(t), U(t + \theta_j - \theta_k))\, dt. \tag{A21}$$

Equation (A21) has the same form as (A10). We prove that $U^{*T}(t) = \chi^*(t)$ is the solution to (A20) and thus show uniqueness of U^* by virtue of the uniqueness of χ^*. This also implies that $\breve{H} = \tilde{H}$. We seek solutions $\chi^*(t)$ to (A20) of the form

$$\chi^*(t) = U'(t)\zeta(t) + M(t)z(t). \tag{A22}$$

Substitution of (A22) into (A20) leads to

$$U''\zeta + U'\zeta' + M'z + Mz' + D^T U'\zeta + D^T Mz = 0. \tag{A23}$$

We multiply (A23) by U'^T and using (A2) we obtain

$$U'^T U''\zeta + \varrho\zeta' + (U'^T M' + U'^T D^T M)z + U'^T D^T U'\zeta = 0. \tag{A24}$$

From $(-U_k')^T M_k' = (U_k')^T (D_k)^T M_k$ and the fact that $U'' = DU'$, we see that (A24) simplifies to

$$(U''^T U' + U'^T U'')\zeta + \varrho\zeta' = 0.$$

Since $(U''^T U' + U'^T U'') = (U'^T U')' = \varrho'$, we have $\varrho'\zeta + \varrho\zeta' = 0$. Along with the normalization condition of (A20) this implies

$$\zeta(t) = \varrho^{-1}(t). \tag{A25}$$

We now multiply (A23) by M^T and, using (A2), obtain

$$z' = -(M^T D^T M + M^T M')z - (M^T U'' + M^T D^T U')\varrho^{-1}. \tag{A26}$$

Again using the fact that $U'' = DU'$ and also (A12), we see that (A26) is just

$$z' = -a^T(t)z - b^T(t). \tag{A27}$$

The fundamental matrix for $z' = -a^T(t)z$ is $E^{-1}(t)^T$ and $z(t)$ is required to be 2π-periodic; thus

$$z(t) = E^{-1}(t)^T\{[I - E(2\pi)^T]^{-1}Q(2\pi)^T - Q^T(t)\}. \tag{A28}$$

Combining (A28) with (A25) and (A23), we see that $\chi^*(t) = U^{*T}(t)$ as required. □

A3. Averaged coupling for neural models

We now wish to apply the results of Sects. A1 and A2 to two-dimensional neural models. The general results in Sects. A1 and A2 of this appendix provide machinery for determining the averaged function $\tilde{H}(\phi)$ for arbitrary weakly coupled oscillators. This task is straightforward once we have chosen coordinates to transform the system of equations into equations of the form (A3). Thus, we must first provide a method for constructing the matrix $M(\theta)$ which satisfies the conditions (A2). In the two-dimensional case, $M(\theta)$ is just a two-dimensional column vector.

Let the components of the limit-cycle for the two-dimensional system be $U(\theta) \equiv (u_1(\theta), u_2(\theta))$. Then $U'(\theta) = (u_1'(\theta), u_2'(\theta))$. We let

$$\varrho(\theta) = \|U'(\theta)\|^2 - u_1'^2(\theta) + u_2'^2(\theta)$$

and choose

$$M(\theta) = (u_2'(\theta), -u_1'(\theta))^T/\sqrt{\varrho(\theta)}.$$

Clearly, this choice satisfies (A2).

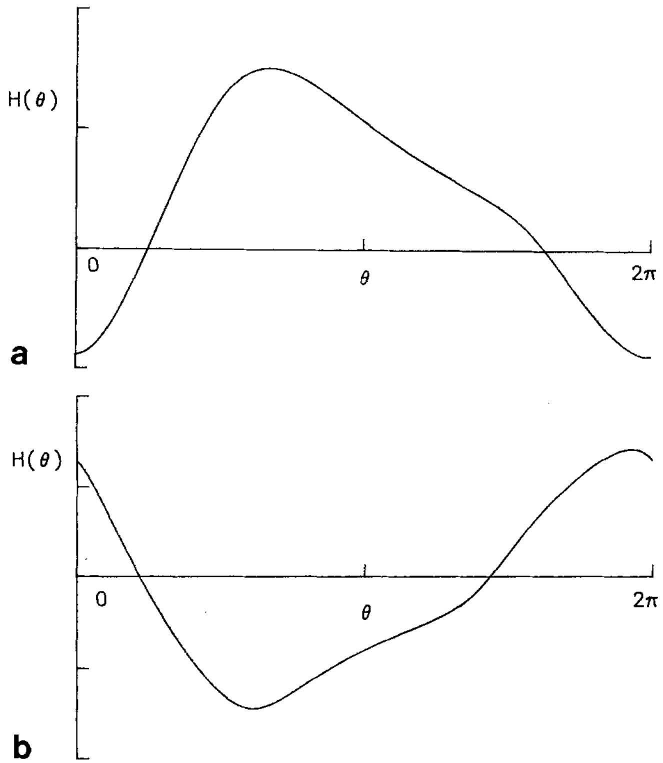

Fig. 10. $H(\theta)$ for Wilson–Cowan equations, $\beta_{ee} = 12$, $\beta_{ie} = 14$, $\beta_{ei} = 18$, $\beta_{ii} = 0$; $f_e(u) = \frac{1}{2}(1 + \tanh(u - \frac{1}{2}))$; $f_i(u) = \frac{1}{2}(1 + \tanh(u - 6))$. **a** excitatory-excitatory coupling; **b** inhibitory-inhibitory coupling

We now use this M to construct $\tilde{H}(\phi)$. Equations (A11) and (A12) are scalar equations that are readily integrated using standard methods. This allows us to easily construct the functions $U^*(\theta)$ defined in (A17) and consequently determine the averaged function $\tilde{H}(\phi)$ for any two-dimensional oscillator.

We have written a computer program for numerical calculation of the function $U^*(\theta)$ which is then used to derive the averaged function for any system of weakly coupled two-dimensional oscillators. In Fig. 10, we plot the averaged functions for two coupled Wilson–Cowan models:

$$\begin{aligned} dE_j/dt &= -E_j + f_e(\beta_{ee}E_j - \beta_{ie}I_j + \alpha_e E_k), \\ dI_j/dt &= -I_j + f_i(\beta_{ei}E_j - \beta_{ii}I_j - \alpha_i I_k), \end{aligned} \tag{A29}$$

for $j, k = 1, 2$ $j \neq k$. In Fig. 10a, we assume that $\alpha_i = 0$ and $0 < \alpha_e \ll 1$, i.e., weak excitatory-excitatory coupling. In Fig. 10b, we assume that $\alpha_e = 0$ and α_i is small and positive, corresponding to weak inhibitory-inhibitory coupling. The slope at the origin determines the stability of the in-phase solution for two coupled identical oscillators. From this, one sees that weak inhibitory-inhibitory coupling always results in unstable in-phase solutions; the stable phase-difference is half a cycle. Weak excitatory-excitatory coupling is more complicated; for identical oscillators, the in-phase solution is not stable, and the stable solution has a small phase-difference. We have verified this by integrating the full equations (A29) for small α_e.

References

1. Glass, L., Mackey, M.: From clocks to chaos: the rhythms of life. Princeton: Princeton University Press 1988
2. Kopell, N. Ermentrout, G. B.: Coupled oscillators and the design of central pattern generators. Math. Biosci. **90**, 87–109 (1988)
3. Friesen, W. O., Poon, M., Stent, G.: Neuronal control of swimming in the medicinal leech IV. Identification of a network of oscillatory interneurons. J. Exp. Biol. **75**, 25–43 (1978)
4. Kopell, N.: Toward a theory of modelling central pattern generators. In: Cohen, A. H., Rossignol, S., Grillner, S. (eds.), The neural control of rhythmic movements in vertebrates, pp. 369–413. New York: Wiley 1987
5. Ermentrout G. B., Rinzel, J. M.: Phase walkthrough in biological oscillators. Am. J. Physiol. **246**, R602–606 (1983)
6. Schrieber, I., Marek, M.: Strange attractors in coupled reaction-diffusion cells. Physica **15d**, 258–272 (1982)
7. Ermentrout, G. B., Kopell, N.: Oscillator death in systems of coupled neural oscillators. SIAM J. Appl. Math., to appear
8. Morris, C., Lecar, H.: Voltage oscillations in the barnacle giant muscle fiber. Biophysical J. **35**, 193–213 (1981)
9. Wilson, H. R., Cowan J. D.: Excitatory and inhibitory interactions in localized populations of model neurons. Biophys. J. **12**, 1–24 (1972)
10. Ermentrout, G. B., Kopell, N.: Frequency plateaus in a chain of weakly coupled oscillators, I. SIAM J. Math. Anal. **15**, 215–237 (1984)
11. Fenichel, N.: Persistence and smoothness of invariant manifolds for flows. Indiana Univ. Math. J. **21**, 193–226 (1971)
12. Sanders, J. A., Verhulst, F.: Averaging methods in nonlinear dynamical systems. (Appl. Math. Sci., vol. **59**) Springer: New York 1985
13. Ermentrout, G. B.: The behavior of rings of coupled oscillators. J. Math. Biol, **23**. 55–74 (1986)
14. Aronson, D. G., Ermentrout, G. B., Kopell, N.: Amplitude response of coupled oscillators. Physica D, to appear